REMARKS

Upon entry of this amendment, claims 1-30 and 33-34 will be pending in the instant application, with claims 13-22 being withdrawn as directed to non-elected subject matter. Claims 1-12, 23, 25-29 and 33 have been amended and claim 34 has been added. Claims 31-32 have been cancelled without prejudice or disclaimer. Applicant reserves the right to pursue the withdrawn and/or cancelled subject matter in one or more continuing applications.

Support for the claim amendments presented herein is found throughout the specification and in the claims as originally filed. For example, support for the amendments to claim 1 is found at least in paragraph **[0044], [0186]** through **[0189]** and in Example 6 of US Patent Application Publication No. 2005/0084449A1. Support for the amendments to claim 2 and for new claim 34 is found at least in Tables 4-5, in Example 4 and in paragraphs **[0093]** and **[0094]** of the '449 publication. Support for the amendments to claim 11 is found at least in paragraph **[0022]**, in Tables 4-5 and 9, and in Examples 4-5 of the '449 publication. Support for the antigen-binding fragments recited by the amended claims is found at least in paragraphs **[0099]** through **[0101]** of the '449 publication. In addition, claims 3-10, 12, 23, 25-29 and 33 have been amended solely to maintain antecedent basis and/or claim dependency throughout the amended claim set. The specification has been amended to ensure that the sequence identifiers throughout the specification match in the substitute sequence listing submitted herewith. Accordingly, the present amendments are fully supported by the original disclosure, and no new matter has been added.

Claim Amendments

Applicant has amended certain claims, *e.g.*, claims 2 and 11, and added new claim 34 to recite specific heavy and light chain complementarity determining region (CDR) combinations and/or specific variable heavy chain and variable light chain combinations as disclosed in Tables 4-5 of the specification as originally filed.

The disclosure in the specification demonstrates that the specific recited combinations of heavy and light chain CDR regions and variable heavy and variable light chain regions bind TIM-1. The CDR regions of antibodies determine the antibody's binding specificity and characteristics, therefore, defining the three CDR regions of the heavy and light chain fully

defines the anti-TIM-1 antibodies. The percentage identity language has been added to these claims to provide Applicant with fair and reasonable scope of protection for the claimed invention. Moreover, the amended claims are not directed to any sequence that is 90% identical to the specific combinations of heavy and light chains recited by the amended claims, but only those that bind TIM-1. Applicant submits that the skilled artisan, without undue burden and using routine skill in the art, would be able to identify the heavy and light chains that fall within the scope of the amended claims.

In addition, the pending claims have been amended to recite antibodies that bind TIM-1 or antigen-binding fragments thereof, which are disclosed in the specification as originally filed, *e.g.*, in paragraph **[0099]**. Thus, the amended claims are not directed to any fragment of an anti-TIM-1 antibody, but only those that bind TIM-1. Applicant submits that the skilled artisan, without undue burden and using routine skill in the art, would be able to identify the fragments that fall within the scope of the amended claims.

Accordingly, Applicant submits that the amended claims presented herein are adequately supported by the disclosure in the instant application.

Sequence Listing

A substitute sequence listing is submitted herewith to correct inadvertent errors in the initial sequence listing as filed on December 16, 2004 in the instant application. In particular, the substitute sequence listing has been amended to ensure that the sequences presented therein are match the sequence identifiers as used throughout the specification as originally filed.

The content of the paper and computer readable forms of the substitute sequence listing submitted herewith in accordance with 37 C.F.R. § 1.821(c) and 1.821(e), respectively, are the same. In addition, the substitute sequence listing is supported by the specification and the sequence identifiers used therein. Accordingly, no new matter has been added by this substitute sequence listing.

Claim Rejections Under 35 U.S.C. § 102

Claims 1, 3-12 and 31 have been rejected under 35 U.S.C. § 102(e), as being anticipated by US Patent Publication No. 2003/0124114 by McIntire et al. ("McIntire").

Independent claim 1 has been amended to recite an isolated human antibody or antigen-binding fragment thereof that specifically binds to human T cell, immunoglobulin domain and mucin domain 1 (TIM-1), wherein the antibody or antigen-binding fragment thereof specifically binds an epitope on TIM-1 comprising the amino acid sequence PMPLPRQNHEPVAT (SEQ ID NO: 87).

McIntire, in contrast, does not teach or suggest any epitopes on the TIM-1 antigen, nor is there any disclosure regarding antibodies that specifically bind to a particular epitope on TIM-1. McIntire does not specifically identify any subportions of the TIM-1 amino acid sequence shown in Figures 5A, 7 and 8. Rather, the claimed epitope sequence, PMPLPRQNHEPVAT (SEQ ID NO: 87), is presented in McIntire only within the context of a full-length TIM-1 polypeptide. There is no teaching or suggestion that any portion of the TIM-1 polypeptide sequence disclosed in McIntire is particularly important for antibody-binding, let alone that the specific claimed sequence (PMPLPRQNHEPVAT) is an epitope for antibody-binding.

Thus, the McIntire reference does not teach any epitopes of TIM-1, let alone the particular epitope recited by amended claim 1 and its dependent claims. In addition, this reference does not describe any antibodies that bind the specific sequence PMPLPRQNHEPVAT. As such, the McIntire reference fails to teach every element of the claimed invention, and this rejection should be withdrawn.

Claim Rejections Under 35 U.S.C. § 103

Claims 1, 3-12 and 23-33 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over the McIntire reference in view of US Patent Application Publication No. 2004/0124114A1 by Watkins et al. ("Watkins").

Applicant traverses the rejection as applied to the amended claims presented herein. As described above, claim 1 has been amended to recite anti-TIM-1 antibodies or antigen-binding fragments thereof that specifically bind an epitope of human TIM-1 that includes the amino acid sequence of SEQ ID NO: 87. In addition, amended claims 2, 11 and new claim 34 are directed

to specific heavy and light chain CDR combinations and/or specific variable heavy chain and variable light chain combinations as disclosed in Tables 4-5 of the specification as originally filed.

The antibodies of the claimed invention bind human TIM-1 and modulate one or more biological activities of TIM-1 as shown throughout the specification, *e.g.*, in Examples 8-10, 12 and 16-18. In contrast, the McIntire and Watkins references, alone or in combination, fail to describe or suggest antibodies that (i) bind a specific epitope of human TIM-1 and/or antibodies that contain the claimed CDR and/or variable heavy and light chain regions and (ii) are able to modulate a biological activity of TIM-1.

The only specific anti-TIM-1 antibodies described in the McIntire reference were generated using murine TIM-1 antigen, and these antibodies are murine anti-TIM-1 antibodies. (*See e.g.*, Examples 4-5 of McIntire). Moreover, this reference does not describe any antibodies that bind an epitope that includes the specific amino acid sequence PMPLPRQNHEPVAT. As described above, the claimed epitope sequence (SEQ ID NO: 87) is presented in McIntire only within the context of a full-length TIM-1 polypeptide. There is no teaching or suggestion that would lead the skilled artisan to identify any particular portion of the TIM-1 polypeptide sequence disclosed in McIntire as more (or less) important for antibody-binding. Thus, the skilled artisan would not be motivated by the teachings of the McIntire reference to produce antibodies that bind any particular sequence within the TIM-1 antigen, let alone antibodies that bind that the specific epitope sequence recited by amended claim 1.

The addition of the Watkins reference fails to cure the deficiencies in the teachings of McIntire, as Watkins does not teach or suggest the human TIM-1 epitope and/or the specific antibody sequences recited by the amended claims. Watkins describes various methods of producing antibodies having optimized heteromeric variable regions, but does not describe any antibodies that bind TIM-1. Thus, there is no teaching or suggestion in Watkins that would clearly lead the skilled artisan to produce any antibodies that bind human TIM-1, let alone antibodies that bind human TIM-1 and modulate at least one biological activity of TIM-1.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one ordinary skill in the art. *See* MPEP §2143.01, citing *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385, 1396 (2007). Furthermore, a statement that modifications of the prior art to meet

the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *See* MPEP §2143.01, citing *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993).

There is no objective reason provided by the McIntire and/or Watkins references that would lead the skilled artisan to combine and modify these references to arrive at the claimed invention, nor is there any evidence that the resultant combination and modification of these references would have been predictable. These references, alone or in combination, fail to provide the skilled artisan with a reasonable expectation that antibodies that possess the claimed characteristics would successfully bind human TIM-1 and modulate one or more biological activities of this target.

Accordingly, any suggestion that it would have been obvious to arrive at the claimed antibodies is an improper application of hindsight based on Applicant's disclosure in the instant application. Applicant submits, therefore, that the Examiner has failed to establish a *prima facie* case of obviousness and request that this rejection be withdrawn.

CONCLUSION

On the basis of the foregoing amendments, Applicant respectfully submits that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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